Abstract

Thesis: Novel Synthesis of Quinoline-5,8-Dione Analogues

Student: Alicen Teitgen

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The chemistry of quinonline-5,8-dione as a functional group is a developing field because of its various biological aspects. Lavendamycin and streptonigrin are known antibiotic, antitumor agents containing the quinolone-5,8-dione functional group believed to provide their antitumor properties. Most cancer cells show an elevated level of NQO1 enzyme which activates lavendamycin to act as an antitumor agent. The research goal is to explore different synthetic methods and reactions to produce novel quinolone-5,8-dione analogues with unique structural features while keeping the selective cytotoxicity. Lavendamycin contains a β-carboline and streptonigrin has a substituted pyridine connected to the 2-position of the quinolone-5,8-dione. The overall goal of this project will develop synthetic methods to create 1,2,3-triazoles and 1,2-diazoles attached to the quinoline moiety from azides and diazonium salts, respectively.

In order to accomplish this, 8-hydroxyquinoline undergoes through a four step synthesis to install an azide at the two position of the quinoline ring. 8-Hydroxyquinoline was oxidized to produce 8-hydroxyquinoline-N-oxide, converted into 8-acetoxy-2-hydroxyquinoline with acetic anhydride, reacted with $POCl_3$ to produce 2-chloro-8-hydroxyquinoline, and treated with sodium azide to form 2-azido-8-hydroxyquinoline. However it was found that the product cyclized to yield 8-hydroxy-tetrazole[1,5-a]quinoline.

In the quinoline-5,8-dione synthesis, 7-amidoquinoline-5,8-dione is prepared through a three step synthesis. 8-Hydroxquinoline was nitrated to form 8-hydroxy-5,7-dinitroquinoline, hydrogenated/acylated to give 5,7-diacetamido-8-acetoxyquinoline, and oxidized to yield 7-acetamidoquinoline-5,8-dione. In order to reach the end of this project, the four step tetrazole and the three step quinoline-5,8-dione syntheses required merging. Further research will focus on the optimization of these syntheses.